



ENDO LABORATORIES

MOBAN®  
(Molindone Hydrochloride)

**Rx only**

## DESCRIPTION

MOBAN (molindone hydrochloride) is a dihydroindolone compound which is not structurally related to the phenothiazines, the butyrophenones or the thioxanthenes.

MOBAN is 3-ethyl-6, 7-dihydro-2-methyl-5-(morpholinomethyl) indol-4 (5H)-one hydrochloride. It is a white to offwhite crystalline powder, freely soluble in water and alcohol and has a molecular weight of 312.67.

MOBAN Tablets also contain:

All strengths: calcium sulfate, lactose, magnesium stearate, microcrystalline cellulose and povidone.

5 mg: alginic acid, colloidal silicon dioxide and FD&C Yellow 6.

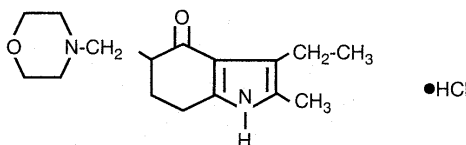
10 mg: alginic acid, colloidal silicon dioxide, FD&C Blue 2 and FD&C Red 40.

25 mg: alginic acid, colloidal silicon dioxide, D&C Yellow 10, FD&C Blue 2, and FD&C Yellow 6.

50 mg: FD&C Blue 2 and sodium starch glycolate.

100 mg: FD&C Blue 2, FD&C Yellow 6 and sodium starch glycolate.

MOBAN Concentrate contains: alcohol, artificial cherry flavor, artificial cover flavor, edetate disodium, glycerin, liquid sugar, methylparaben, propylparaben, sodium metabisulfite, sorbitol solution, and hydrochloric acid reagent grade for pH adjustment.



MOLINDONE HYDROCHLORIDE

## CLINICAL PHARMACOLOGY

MOBAN has a pharmacological profile in laboratory animals which predominantly resembles that of other antipsychotic agents causing reduction of spontaneous locomotion and aggressiveness, suppression of a conditioned response and antagonism of the bizarre stereotyped behavior and hyperactivity induced by amphetamines. In addition, MOBAN antagonizes the depression caused by the tranquilizing agent tetrabenazine.

In human clinical studies an antipsychotic effect is achieved in the absence of muscle relaxing or incoordinating effects. Based on EEG studies, MOBAN exerts its effect on the ascending reticular activating system.

Human metabolic studies show MOBAN to be rapidly absorbed and metabolized when given orally. Unmetabolized drug reached a peak blood level at 1.5 hours. Pharmacological effect from a single oral dose persists for 24-36 hours. There are 36 recognized metabolites with less than 23% unmetabolized MOBAN being excreted in urine and feces.

## INDICATIONS AND USAGE

MOBAN is indicated for the management of schizophrenia. The efficacy of MOBAN in schizophrenia was established in clinical studies which enrolled newly hospitalized and chronically hospitalized, acutely ill, schizophrenic patients as subjects.

## CONTRAINDICATIONS

MOBAN is contraindicated in severe central nervous system depression (alcohol, barbiturates, narcotics, etc.) or comatose states, and in patients with known hypersensitivity to the drug.

## WARNINGS

### Tardive Dyskinesia

Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be

highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, antipsychotics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

(For further information about the description of tardive dyskinesia and its clinical detection, please refer to the section on Adverse Reactions.)

### **Neuroleptic Malignant Syndrome (NMS)**

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include, 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

### **Pregnancy**

Studies in pregnant patients have not been carried out. Reproduction studies have been performed in the following animals:

#### **Pregnant Rats oral dose**

no adverse effect	20 mg/kg/day-10 days
no adverse effect	40 mg/kg/day-10 days

#### **Pregnant Mice oral dose**

slight increase resorptions	20 mg/kg/day-10 days
slight increase resorptions	40 mg/kg/day-10 days

#### **Pregnant Rabbits oral dose**

no adverse effect	5 mg/kg/day-12 days
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no adverse effect 10 mg/kg/day-12 days

no adverse effect 20 mg/kg/day-12 days

Animal reproductive studies have not demonstrated a teratogenic potential. The anticipated benefits must be weighed against the unknown risks to the fetus if used in pregnant patients.

### **Nursing Mothers**

Data are not available on the content of MOBAN (molindone hydrochloride) in the milk of nursing mothers.

### **Pediatric Use**

Use of MOBAN in pediatric patients below the age of twelve years is not recommended because safe and effective conditions for its usage have not been established.

MOBAN has not been shown effective in the management of behavioral complications in patients with mental retardation.

### **Sulfites Sensitivity**

MOBAN Concentrate contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

## **PRECAUTIONS**

### **General**

Some patients receiving MOBAN may note drowsiness initially and they should be advised against activities requiring mental alertness until their response to the drug has been established.

Increased activity has been noted in patients receiving MOBAN. Caution should be exercised where increased activity may be harmful.

MOBAN does not lower the seizure threshold in experimental animals to the degree noted with more sedating antipsychotic drugs. However, in humans convulsive seizures have been reported in a few instances.

The physician should be aware that this tablet preparation contains calcium sulfate as an excipient and that calcium ions may interfere with the absorption of preparations containing phenytoin sodium and tetracyclines.

MOBAN has an antiemetic effect in animals. A similar effect may occur in humans and may obscure signs of intestinal obstruction or brain tumor..

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

### **Drug Interactions**

Potential of drugs administered concurrently with MOBAN has not been reported. Additionally, animal studies have not shown increased toxicity when MOBAN is given concurrently with representative members of three classes of drugs (i.e., barbiturates, chloral hydrate and antiparkinson drugs).

## **ADVERSE REACTIONS CNS Effects**

The most frequently occurring effect is initial drowsiness that generally subsides with continued usage of the drug or lowering of the dose.

Noted less frequently were depression, hyperactivity and euphoria.

### **Neurological**

#### **Extrapyramidal Reactions**

Extrapyramidal reactions noted below may occur in susceptible individuals and are usually reversible with appropriate management.

#### **Akathisia**

Motor restlessness may occur early.

### **Parkinson Syndrome**

Akinesia, characterized by rigidity, immobility and reduction of voluntary movements and tremor, have been observed. Occurrence is less frequent than akathisia.

### **Dystonic Syndrome**

Prolonged abnormal contractions of muscle groups occur infrequently. These symptoms may be managed by the addition of a synthetic antiparkinson agent (other than L-dopa), small doses of sedative drugs, and/or reduction in dosage.

### **Tardive Dyskinesia**

Antipsychotic drugs are known to cause a syndrome of dyskinetic movements commonly referred to as tardive dyskinesia. The movements may appear during treatment or upon withdrawal of treatment and may be either reversible or irreversible (i.e., persistent) upon cessation of further antipsychotic administration.

The syndrome is known to have a variable latency for development and the duration of the latency cannot be determined reliably. It is thus wise to assume that any antipsychotic agent has the capacity to induce the syndrome and act accordingly until sufficient data has been collected to settle the issue definitively for a specific drug product. In the case of antipsychotics known to produce the irreversible syndrome, the following has been observed.

Tardive dyskinesia has appeared in some patients on long-term therapy and has also appeared after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). There may be involuntary movements of extremities.

There is no known effective treatment of tardive dyskinesia; antiparkinsonism agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, the syndrome may be masked. It has been reported that fine vermicular movements of the tongue may be an early sign of the syndrome and if the medication is stopped at that time the syndrome may not develop (See WARNINGS).

### **Autonomic Nervous System**

Occasionally blurring of vision, tachycardia, nausea, dry mouth and salivation have been reported. Urinary retention and constipation may occur particularly if anticholinergic drugs are used to treat extrapyramidal symptoms. One patient being treated with MOBAN (molindone hydrochloride) experienced priapism which required surgical intervention, apparently resulting in residual impairment of erectile function.

### **Laboratory Tests**

There have been rare reports of leucopenia and leucocytosis. If such reactions occur, treatment with MOBAN may continue if clinical symptoms are absent. Alterations of blood glucose, B.U.N. and red blood cells have not been considered clinically significant.

### **Metabolic and Endocrine Effects**

Alteration of thyroid function has not been significant. Amenorrhea has been reported infrequently. Resumption of menses in previously amenorrheic women has been reported. Initially heavy menses may occur. Galactorrhea and gynecomastia have been reported infrequently. Increase in libido has been noted in some patients. Impotence has not been reported. Although both weight gain and weight loss have been in the direction of normal or ideal weight, excessive weight gain has not occurred with MOBAN.

### **Hepatic Effects**

There have been rare reports of clinically significant alterations in liver function in association with MOBAN use.

### **Cardiovascular**

Rare, transient, non-specific T wave changes have been reported on E.K.G. Association with a clinical syndrome has not been established. Rarely has significant hypotension been reported.

### **Ophthalmological**

Lens opacities and pigmentary retinopathy have not been reported where patients have received MOBAN. In some patients, phenothiazine induced lenticular opacities have resolved following discontinuation of the phenothiazine while continuing therapy with MOBAN.

### **Skin**

Early, non-specific skin rash, probably of allergic origin, has occasionally been reported. Skin pigmentation has not been seen with MOBAN usage alone.

MOBAN has certain pharmacological similarities to other antipsychotic agents. Because adverse reactions are often extensions of the pharmacological activity of a drug, all of the known pharmacological effects associated with other antipsychotic drugs should be kept in mind when MOBAN is used. Upon abrupt withdrawal after prolonged high dosage an abstinence syndrome has not been noted.

### **OVERDOSAGE**

Symptomatic, supportive therapy should be the rule.

Gastric lavage is indicated for the reduction of absorption of MOBAN which is freely soluble in water.

Since the adsorption of MOBAN by activated charcoal has not been determined, the use of this antidote must be considered of theoretical value.

Emesis in a comatose patient is contraindicated. Additionally, while the emetic effect of apomorphine is blocked by MOBAN in animals, this blocking effect has not been determined in humans.

A significant increase in the rate of removal of unmetabolized MOBAN from the body by forced diuresis, peritoneal or renal dialysis would not be expected. (Only 2% of a single ingested dose of MOBAN is excreted unmetabolized in the urine). However, poor response of the patient may justify use of these procedures.

While the use of laxatives or enemas might be based on general principles, the amount of unmetabolized MOBAN in feces is less than 1 %. Extrapyramidal symptoms have responded to the use of diphenhydramine (Benadryl)\*, Amantadine HCl (Symmetrel) and the synthetic anticholinergic antiparkinson agents, (i.e., Artane, Cogentin, Akineton).

### **DOSAGE AND ADMINISTRATION**

Initial and maintenance doses of MOBAN (molindone hydrochloride) should be individualized.

#### **Initial Dosage Schedule**

The usual starting dosage is 50-75 mg/day.

- Increase to 100 mg/day in 3 or 4 days.

- Based on severity of symptomatology, dosage may be titrated up or down depending on individual patient response.

- An increase to 225 mg/day may be required in patients with severe symptomatology.

Elderly and debilitated patients should be started on lower dosage.

#### **Maintenance Dosage Schedule**

1. Mild-5 mg-15 mg three or four times a day.

2. Moderate-10 mg-25 mg three or four times a day.

3. Severe-225 mg/day may be required.

### **HOW SUPPLIED**

As tablets in bottles of 100 with potencies and colors as follows:

5 mg	Orange, round, biconvex tablet, one face inscribed with NDC 63481-072-70 "Moban 5", and the other face plain.
10 mg	Lavender, round, biconvex tablet, one face inscribed with NDC 63481-073-70 "Moban 10", and the other face plain.
25 mg	Green, round, biconvex tablet, one face scored and NDC 63481-074-70 inscribed with "Moban 25", and the other face plain with partial bisect.
50 mg	Blue, round, biconvex tablet, one face scored and NDC 63481-076-70

inscribed with "Moban 50", and the other face plain.

100 mg                      Tan, round, biconvex tablet, one face scored andNDC 63481-077-70  
inscribed with "Moban 100", and the other face plain.

As a concentrate (clear, colorless to straw-yellow syrup) containing 20 mg molindone hydrochloride per mL in 4 oz. (120 mL) bottles, NDC 63481-460-04.

Store at controlled room temperature 15°-30° C (59°-86° F). Protect from light.

Benadryl is a registered trademark of Warner-Lambert.

Symmetrel is a registered trademark of Endo Pharmaceuticals Inc.

Artane is a registered trademark of Lederle Laboratories.

§Cogentin is a registered trademark of Merck & Co., Inc.

Akineton is a registered trademark of Knoll Laboratories.

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